DRAFT DOCUMENT

PEST MANAGEMENT REGULATORY AGENCY
HEALTH CANADA

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Electronic Dossier, Delivery, and Evaluation	Livraison, Evaluation, Dossier Electronic

PRELIMINARY STATEMENT OF EVALUATOR REQUIREMENTS

25 June 1999

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1.0 INTRODUCTION

This Guidance Document contains Annexes which outline requirements based on the applicable Acts, Regulations, and working procedures and address such issues such as Electronic Dossier assembly and provision of electronic data formats that will contribute to the efficiency of PMRA evaluators. During the PMRA Electronic Dossier, Delivery, and Evaluation (EDDE) Pilot Stage these will be refined, validated and finalized.

2.0 FUNCTIONALITY

This section discusses characteristics of the electronic tools used to access electronic Dossiers. Guidance is given concerning features considered necessary of tools to permit efficient use by evaluators in the PMRA.

In developing the guidance, the goal of the PMRA is to establish a neutral Dossier transmission package which neither imposes a requirement of industry to use proprietary software for the production, assembly, and delivery of electronic data, nor obligates the PMRA to maintain, and train staff on, a large variety of electronic tools to access data, evaluate data, and produce evaluation reports and subsequent regulatory publications. The Dossier transmission package (combination of electronic data file format(s) and data access tools) chosen for delivery of electronic Dossiers must be designed to support the efficient electronic review of the Dossier. Electronic data file formats and data access tools will be evaluated against their ability to efficiently satisfy identified evaluator needs. Therefore, the data access tool and the electronic data file format need to be considered together.

2.1 Evaluator identified functionality needs

Evaluators have indicated that, in an integrated electronic Dossier delivery and evaluation environment, evaluation efficiency can be improved by ensuring that the chosen electronic Dossier transmission package provides the functional abilities identified below. These functional abilities are closely related to Software properties discussed later (section 4.2.2).

- **!** Viewing
  Easily view a clear and legible copy of the information on the PMRA minimum standard 17" monitor
  Ability to open multiple page views simultaneously
  NOTE: The PMRA is evaluating the utility of alternate monitor setups for electronic evaluation of Dossier data. Larger 21" monitors are currently being tested with an evaluator team during evaluation of a current electronic Dossier. A dual 17" monitor workstation is available to all staff

for trial.

- **!** Navigation/drill down
  Navigation tools should apply at the Dossier and single study level.

- **!** Full text/context searching
  Within study minimum, between studies (DACO group or Dossier level beneficial)

- **!** Online annotation/bookmarking
  Prefer ability to write back to working evaluation copy of the submitted dossier in a LAN based Dossier to enable sharing of annotations/bookmarks between evaluators

- **!** Opportunity to access non-traditional information (images, video, etc)

- **!** Report generation capabilities
  Re-use/re-purposing of data
    Accurate copy and paste of all data types including, minimally, text, tables, and image data.
  Data manipulation/testing
    It should be possible to paste text data to word processing packages and tabular data to word processing and spreadsheet applications

- **!** Printing to 8.5" x 11" paper

2.2 Data access tool functionality

2.2.1 PMRA IT environment considerations

2.2.1.1 The PMRA does not endorse any particular software application or software vendor that Applicants may use to assemble an electronic Dossier.

2.2.1.2 Software utilized to access electronic data must be compatible with the PMRA LAN system. See Annex IV for a current description of the PMRA LAN and typical desktop configuration. The information presented in Annex IV will be updated periodically. The impact of any data transmission package on LAN traffic must be a consideration in any proposed solution.

2.2.1.3 The Dossier must be software neutral to the PMRA. E.g. any web browser could be used to view data in a web-based solution.

2.2.1.4 The PMRA will not purchase or maintain any software which may be required as part of any Dossier data access tool. If specific software components are required to access an electronic Dossier, the Applicant is expected to provide these to the PMRA at no cost. See Annex IV for a list of software the PMRA currently maintains for its internal business purposes.

2.2.1.5 As part of any pre-submission consultation, Applicants should identify the software involved to ensure that, if necessary, the PMRA has sufficient time and resources to appropriately train staff.

2.2.2 Software properties

The software used to provide access to electronic data should have the following characteristics.

2.2.2.1 Ease of use

Data access tools should be designed to intuitive. The adoption and use of standard Windows interfaces in any data access tool should ensure that training is minimal.

2.2.2.2 Security

The software must have a password protection feature.

2.2.2.3 Viewing

- Enable user to easily view a clear and legible copy of the information. The standard page view should provide legible text of a size which minimizes the necessity to scroll the screen view to view an entire page on a standard 17" monitor. True Type, 12 point, non-serif fonts generally provide legible on-screen documents.

- An option should be available to enable continuous Page view scrolling, or discontinuous page at a time view scrolling.

- User should be able to change page rotation and magnification.

- Provide the ability to open multiple (independent) page views.

2.2.2.4 Navigation

The software must have comprehensive navigation tools which provide as much of the following as possible, as noted or equivalent:

- Table of Contents.
  A Dossier Table of Contents should be available as a navigation tool. The Table of Contents should have attempt to provide the following

characteristics:

- Organized (Directory branch titles) by DACO number.
- An expandable/collapsible directory structure.
- Table of Contents entries function as link to documents.
- Extends to the level of study report sections, and contains tables and figures lists.
- Contains supplemental data file directory.
- Opened as a window to enable toggle of full screen view of a document/index.
- Always reflects current position in the dossier for the selected view window.
- Use full study title or identifying detail instead of a general descriptor
- Ability to text search index.

! Study title in the window title bar which reflects the study report being viewed.
This is a desirable feature because some evaluators have noted that, after a number of hyperlink movements or go-to page commands, it is easy to get lost in a study or Dossier.

! Full text/context searching.
Within study minimum, between studies (Dossier level preferred).

! Page advance/back.

! Go to page feature.

! Access to alternate format data files included in the Dossier
Direct access from the principle data access tool to the supplementary data is the preferred option. Supplementary data is defined as data included in an electronic Dossier which is in a data file format different from the file format of the main body of electronic data.

! Hypertext linking (with return to link source or previous view feature).
Required hypertext linking:

- For each item in Dossier indices (Dossier and individual study), including all tables, figures, publications, and appendices.
- Linking provided throughout the body of the document to related sections, appendices, tables, or figures that are not located on the same page. For example, this type of linking includes links from text references to supporting data, and from a summary data table to its supporting individual animal data tables.
- Electronically supplied PMRA screening forms should be

hyperlinked from each box in the form to the relevant data element to facilitate electronic screening.

Optional hypertext linking possibilities include, in descending order of preference:
- from Tier II Comprehensive Data Summaries to the relevant sections within source study reports.

2.2.2.5 Manipulation

Data manipulation tools include accurate copy/paste of text, tables, and images, to either word processor applications for production of evaluation reports, or to spreadsheet applications to permit reorganization of tabular data, and/or recalculation of data measures/summary figures. Ideally, original calculation formulas would be available for examination.

2.2.2.6 Annotation and bookmarks

The ability to create, search, and collate annotations and bookmarks within the electronic data package is desirable. It is preferred, for LAN based tools, that these records be created at the server level on the evaluation copy of the Dossier rather than on individual desktop PC's.

2.2.2.7 Printing

Software must allow printing of selected text, pages, or ranges of pages as it would have been provided on paper, maintaining fonts and special characters, special orientations, table formats and page numbers. For documents formatted for European A4 paper software should also contain a 'shrink to fit' feature to permit printing on North American 8.5" x 11" paper without alteration of document pagination.

2.2.2.8 Dossier version control

For subsequent data submissions affecting the original Dossier, a cover letter which clearly identifies which previously submitted data has been altered, and which clearly identifies data new to the Dossier. The physical media should be clearly marked with the appropriate version number, as noted in section 4.2.2.4.

In addition to physical identification on submitted media, software should provide a means to track Dossier versions. The following are considerations in provision of version control:

! Original data submitted must be preserved.

! Software should provide the ability to incorporate additional or new data into the installed Dossier electronic data.

- **!** Consideration should be given to the ability to copy annotations and bookmarks to an updated study electronic data file.

3.0 ELECTRONIC DATA ORGANIZATION

3.1 Data, paper and electronic, should be organized and indexed in the same manner, in accordance with PMRA requirements. Use of PMRA DACO format, or the OECD format is acceptable.

3.2 Electronic versions of screening forms should be inserted in electronic Dossiers at the end of each study report. This will avoid alteration of study page numbering as compared to the paper version.

3.3 For individual file naming conventions and directory structures for storage of electronic data files, see Annex I.

4.0 ELECTRONIC DATA FILES AND DATA FORMAT

This section discusses characteristics of the electronic data contained in electronic Dossiers. Guidance is given concerning data file format features considered necessary to permit efficient use by evaluators in the PMRA.

In developing the guidance, the goal of the PMRA is to establish a neutral Dossier transmission package which neither imposes a requirement of industry to use proprietary software for the production, assembly, and delivery of electronic data, nor obligates the PMRA to maintain, and train staff on, a large variety of electronic tools to access data, evaluate data, and produce reports. The package (combination of electronic data file format(s) and data access tools) chosen for delivery of electronic Dossiers must be designed to support the efficient electronic evaluation of the Dossier. Electronic data file formats and data access tools will be evaluated against their ability to efficiently satisfy identified evaluator needs. Therefore, the data access tool and the electronic data file format need to be considered together.

In addition, it is a goal of the PMRA to establish a neutral electronic data file format which permits long term archiving of electronic data without the need to also archive a specific data access tool or data access tool version. PDF and HTML/SGML/XML data file format are the format of choice for exchange of information on the Internet. These data file formats are considered to be neutral data file exchange formats because they permit document generation applications to differ from document access applications without the potential loss of information associated with format conversion.

4.1 General considerations

4.1.1 File size limitations

If a data file must be completely loaded at once, data file sizes should be limited to ensure that they can be used efficiently without negatively affecting the performance of desktop PC's. In a LAN application, if the software serves 'page at a time' or portions of a document to the desktop, data file size is less of a concern.

4.1.2 Data file format

4.1.2.1 Choice of data file format

The data file format must be chosen such that PMRA evaluators are able to re-use the electronic data supplied to produce evaluation reports. Applicants should ensure that the data file format chosen permits accurate transfer of all types of data (text, tabular, graphical) to word processing or spreadsheet applications without loss or alteration of data, including font formats (super/subscript, Greek characters, mathematical characters) and footnoted text.

4.1.2.2 Types of data file format

Two types of electronic data file formats are likely to be included in any electronic Dossier. These include the principal electronic data format (a neutral data format for transfer to the PMRA ie PDF, XML) and alternate electronic data formats (native application electronic data format ie Wordperfect, Excel, etc.). In principle, it is desirable that the entire content of an electronic Dossier be of a single data format, the principle electronic data format, to avoid the requirement to maintain and have several viewer programs open. However, it is recognized that, in some cases, the use of an alternate data format would be beneficial for data evaluation purposes. When included in an electronic Dossier, alternate data format files should be clearly identified in the body of the Dossier as being present, be readily accessible, and, if applicable, its location clearly identified. Direct access from the principal data access tool to the alternate data format file is the preferred option. Direct access can include the launching of an appropriate viewing software. PDF, TIFF and equivalents are not considered to be native data format files. See Annex IV for a listing of alternate data file formats which can be utilized by the PMRA.

4.1.2.3 Data file format conversion

Where it is deemed desirable to supply a native data format file, it is the Applicants responsibility to ensure that the format supplied to the PMRA can be used by the PMRA. Where a conversion of data formats by the Applicant is necessary, it is the Applicants responsibility to ensure that the conversion did not result in changes to the data. In particular, Applicants should ensure that items such as footnotes do not get dropped from documents. Where file conversion must performed by the PMRA, the PMRA cannot be held accountable for any unintentional alteration of the supplied data.

4.1.3 Presentation of data

The following items apply to presentation of electronic data in all electronic data formats.

4.1.3.1 Page orientation

Pages should be properly oriented. For example, set the page orientation of landscape pages to landscape so that no page rotation is necessary to view the page when it is displayed by the data access tool.

4.1.3.2 Page margins

The print area for pages should fit on a sheet of paper that is 8.5 inches by 11 inches. Allow a margin of 1 inch on all sides.

4.1.3.3 Fonts

Where possible, in the electronic Dossier data files:

- The number of fonts used in a document should be minimized.
- Use True Type or Adobe Type I fonts
- Select fonts from the following list:
  Times New Roman, Courier, Ariel or fonts installed with Windows 95
- Avoid customized fonts
- Embed fonts when possible

The above considerations for font will help to minimize difficulties associated with font substitution when data files are accessed by PMRA evaluation staff. Use of a black font colour is recommended. Blue font or a blue box may be used for hypertext links. If a font colour other than black is used, avoid light colours that do not print well on grayscale printers.

4.1.3.4 Superscripts

The use of numerical superscripts should be avoided when placed on numerical data, especially in tabulated numerical data. When fonts are not embedded in the electronic data files, and the font used does not exist on an PMRA computer, software packages make font substitutions. When this occurs, superscripts are often dropped to normal text, with the result that the superscript number becomes part of the numerical value it was placed on.

4.1.3.5 Tables

It is important to ensure that tabular presentation of data uses clear row-column

format. Tables which are not clearly presented in row-column format, with individual data elements in individual cells, are often not cleanly transferred from the Dossier study report to the PMRA evaluation report. See also Annex IV Desirable electronic files and other review aids, Spreadsheets. When presenting data in a table, avoid the use of cell shading where the document must be scanned from paper. Cell shading interferes with the readability of images and may interfere with our ability to copy the table text to WordPerfect.

4.1.3.6 Use of PMRA supplied review templates

The PMRA has developed review templates for all studies. The templates are based on US-EPA Data Evaluation Report (DER) templates and are being considered by the OECD Pesticide Forum as a stand alone document. These templates are intended for use in the generation of Comprehensive Data Summary Tier II study summary reports by Applicants and are intended to form the base document for the production of PMRA evaluation reports. Use of these templates for production of electronic Dossiers will further enhance the use of electronic Dossier data and efficiency of evaluation report production. These templates are available electronically upon request.

5.0 PILOT RESULTS

Results specific to each pilot will be made available to the individual Applicant. General results for electronic Dossier delivery and evaluation will be made available to all Applicants.

6.0 PMRA CONTACTS

For advice or clarification of issues related to electronic Dossiers contact either

Cameron Bowes
Room E555
Sir Charles Tupper Building,
2250 Riverside Drive,
Address Locator: 6605E
Ottawa, Ontario, K1A 0K9
ph: 613-736-3514
fx: 613-736-3505
email: cbowes@pmra-arla.hc-sc.gc.ca

Carmen Krogh
Room D746
Sir Charles Tupper Building,
2250 Riverside Drive,
Address Locator: 6607D
Ottawa, Ontario, K1A 0K9
ph: 613-736-3696
fx: 613-736-3699
email: ckrogh@pmra-arla.hc-sc.gc.ca

Copies of guidance documents will be provided on the PMRA web site: http://www.hc-sc.gc.ca/pmra.arla

Annex I: Data file naming and supplemental files guidance

1.0 Principal data file storage and naming conventions

The applicability of the following guidance on the PMRA data file format naming convention is dependent on the necessity of PMRA staff to directly use file names as a means to locate and identify individual data files.

1.1 Where the Dossier data access tool provides the means to locate and identify individual data files, no specific data file directory organization or naming convention needs to be followed. The PMRA LAN and software supports the use of long file names. However, the PMRA will be making electronic templates available Applicants for use in compiling Tier II Comprehensive Data Summaries. It should be possible to easily locate and copy these files. Template file names should not be altered from the names supplied.

1.2 Where PMRA staff must directly use file names to locate and identify individual data files, use of specific file storage and naming conventions is recommended to help avoid misunderstandings, improve communication, and speed the review of a Dossier.

1.2.1 Directory structure and naming convention

To facilitate location of data files, files should be organized by DACO category and number, as identified in Regulatory Directive 98-02. Please use the directory structure outlined in Figure 1 below, to group files within the \[new chem name] directory. The additional \Files sub-directory is not necessary. Figure 1 also contains an example breakdown under the main directory headings. The depth of directory structure necessary should be guided by the number of files included and what is necessary to easily locate particular files. Files which may be requested or included which are not assigned a DACO number, may be included in the base \[new chem name] directory. In this circumstance, include an ASCII or PDF file named README.TXT/PDF to explain what these additional files are.

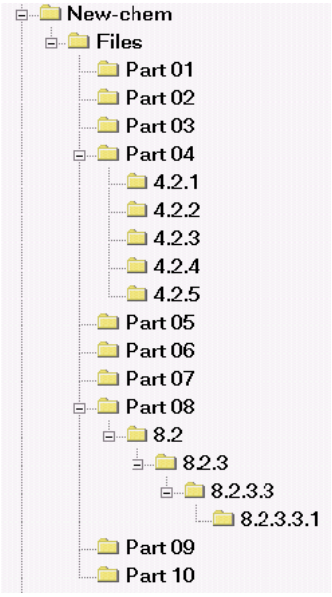


Figure 1: \Files directory structure

1.2.2 File naming convention
General:

- **!** Avoid using punctuation, spaces, or other non-alphanumeric symbols in file names.

- **!** Some filename extensions are registered and have specific meaning in applications, DOS, or Windows. Some of these include .BAT, .COM, .DLL, .EXE, .FIL, .HLP, .INI, .PFC, .REG, .DOC, .WCM, and .WPT. You should not use these extensions when saving documents unless you have a specific reason for doing so.

  A standard file naming convention which takes advantage of long file name support and which will support a number of internal processes is still under development. In the interim; the following file name format should be followed:

  [technical active common name or formulated product designation/name]_[daco number without punctuation]_[letter designation for multiple items under daco]_[study type]_[species if applicable]

  ie For technical active Killall, DACO 4.2.1 acute oral toxicity study in mouse where there is also an acute oral toxicity study for rats, the file name would be

  killall_421_b_acuteoral_mouse

2.0 Supplemental files guidance

Supplemental electronic files such as data bases, spreadsheets, text files, and images which supplement the study reports may also be included with electronic Dossiers. Supplemental, alternate electronic data format files may contain only the information found in the Dossier, but in a different format. Examples of desirable file formats are presented in Annex IV. Corresponding to each data requirement is a listing of file types data evaluators find useful in conducting their evaluations. Guidance regarding acceptable formats of these types of files is not expected to remain static. This guidance will be updated periodically to coincide with advances in available technology and software versions and will be made available on the PMRA web site (http://www.hc-sc.gc.ca/pmra.arla). The applicability of the following guidance will depend to some extent on the tools used to provide access to the data files.

2.1 Location

These files should be contained within a separate directory named \FILES sub-directory under the main \[new chem name] directory. Place the \FILES directory on the index (first) volume of a CD-ROM set. This permits easier location of the files, especially when numerous volumes are included in a CD-ROM set.

2.2 Directory naming and structure
See Annex I, section 1.2.1

2.3 Naming supplemental data files
See Annex I, section 1.2.2

Annex II: CADDY Dossiers

Although CADDY format electronic Dossiers will be accepted, the CADDY system is not considered an adequate tool for evaluation purposes. The archive standard has not yet been determined. A CADDY format electronic Dossier will not, at this time, serve as an archive record.

1.0 General

Information and software relating to the production of a CADDY registration petition package is available on the Internet at the Global Crop Protection Federation site http://www.gcpf.org/. CADDY CD sets must comply with the most recent CADDY Format Specification available at the time of assembly.

All normal regulatory requirements for a paper-based Dossier to the PMRA apply. Delivery of EU formatted CADDY Dossiers must be discussed during pre-submission consultation.

2.0 Supplemental files guidance

Supplemental electronic files such as data bases, spreadsheets, text files, and images which supplement the study reports may also be included with CADDY CD sets. Supplemental, alternate electronic data format files may contain only the information found in the Dossier, but in a different format. Examples of desirable file formats are presented in Annex IV. Corresponding to each data requirement is a listing of file types data evaluators find useful in conducting their evaluations. Guidance regarding acceptable formats of these types of files is not expected to remain static. This guidance will be updated periodically to coincide with advances in available technology and software versions and will be made available on the PMRA web site .

2.1 Location

These files must be contained within the \FILES directory as specified in the CADDY Format Specification document. Although the CADDY Format Specification states that the \FILES directory may be located on any volume of a CD set, placing the directory consistently on the index volume allows for easier location of the files, especially when numerous volumes are included in a CD set.

2.2 Directory naming and structure

To facilitate location of files, Supplemental Files should be organized by DACO category and number, as identified in Regulatory Directive 98-02. Please use the following directory structure, Figure 1, to group files within the \FILES directory. Figure 1 also contains an example breakdown under the main

directory headings. The depth of directory structure necessary should be guided by the number of files included and what is necessary to easily locate particular files. Other files which may be requested or included which are not assigned a DACO number may be included in the base \FILES directory. In this circumstance, include an ASCII or PDF file named README.TXT/PDF to explain what these additional files are.(See naming convention in Annex I)

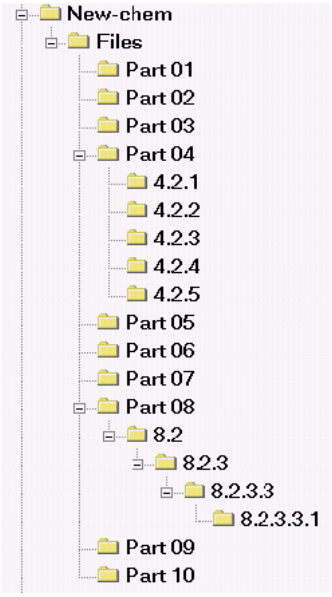


Figure 1: \Files directory structure

2.3 Naming data files

See Annex I.

Annex III: Principle electronic data file format options

This Annex provides a non-exclusive list of data file formats which could be used to provide an electronic Dossier. General guidance is given for each listed file format to help minimize difficulties which may arise during electronic evaluation of the Dossier. This Annex will be updated as difficulties and solutions are identified with each file format.

1.0 PDF: Portable document format

Not all of the following general guidance will apply. The applicability of each section will depend to some extent on the tools used to access the data. If clarification is required, please contact the PMRA.

1.1 Fonts

PDF viewing software automatically substitutes a font to display text if the font used to create the text is unavailable on the reviewers computer. Font substitution can affect a documents appearance and structure, and in some cases it can affect the information conveyed by a document. The PMRA cannot guarantee the availability on any one font. Therefore, all fonts used should be embedded in the PDF files to ensure that those fonts will always be available to the reviewer. When embedding fonts, all characters for the font should be embedded, not just a subset of the fonts being used in the document.

One problem associated with embedding fonts is that embedding requires additional computer storage space. Three techniques to help limit the storage space taken by embedding fonts include:

- limiting the number of fonts used in each document
- using only True Type or Adobe Type I fonts
- Avoiding customized fonts

Use of a black font colour is recommended. Blue font may be used for hypertext links. If a font colour other than black is used, avoid light colours that do not print well on grayscale printers.

1.2 Page Orientation

Pages should be properly oriented. For example, set the page orientation of landscape pages to landscape prior to saving the PDF document in final form to ensure correct page presentation.

1.3 Page Size and Margins

The print area for pages should fit on a sheet of paper that is 8.5 inches by 11 inches. Allow a margin of 1 inch on all sides.

1.4 Source of electronic document

PDF documents produced by scanning paper documents are usually inferior to those produced from an electronic source document. Scanned documents are more difficult to read and do not allow search or copy and past text for editing. They should be avoided if at all possible. If OCR software is used, Applicants must verify that all imaged text converted by the software is accurate.

1.5 Methods for Creating PDF Documents and Images

Choose a method for creating PDF documents that produces the best replication of the original paper document. Documents that are available only in paper should be scanned at resolutions that will ensure the pages are legible both on the computer screen and when printed. At the same time, limit the file size. Scanning at a resolution of 300 dots per inch (dpi) provides a good balance of legibility and file size. After scanning, avoid resampling to a lower resolution. When creating PDF files containing images, resampling images should be avoided. Resampling does not preserve all of the pixels in the original.

Paper documents containing handwritten notes should be scanned at 300 dpi. For photographs, the image should be obtained with a resolution of 600 dpi. If black and white photos are submitted, consider 8-bit gray scale images. If colour photos are submitted, consider 24-bit RGB images. A captured image must not be subjected to non-uniform scaling (i.e., sizing). Gels and karyotypes should be scanned directly, rather than from photographs. Scanning should be at 600 dpi and 8-bit grayscale depth. Plotter output graphics should be scanned or captured digitally at 300 dpi. High-pressure liquid chromatography or similar images should be scanned at 300 dpi.

1.6 Hypertext Linking and Bookmarks

Hypertext links and bookmarks are techniques used to improve navigation through PDF documents. Hypertext links can be designated by rectangles using thin lines or by blue text. Invisible rectangles for hypertext links in a table of contents can be used to avoid obscuring text. In general, for documents with a table of contents, provide bookmarks and hypertext links for each item listed in the table of contents including all tables, figures, publications, other references, and appendices. In general, including a bookmark to the main table of contents for a Dossier is helpful. Make the bookmark hierarchy identical to the table of contents. Avoid using bookmark levels in addition to those present in the table of contents. Each additional level increases the need for space to read the bookmarks. We recommend using no more than 4 levels in the hierarchy.

Use relative paths when creating hypertext linking to minimize the loss of hyperlink functionality when folders are moved between disk drives. Absolute links that reference specific drives and root directories will no longer work once

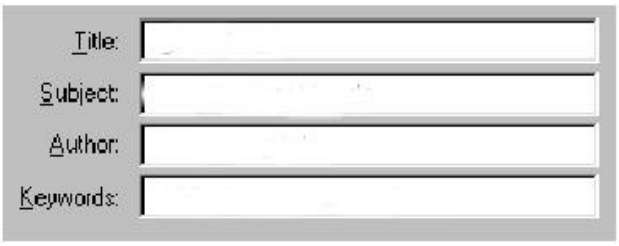
the Dossier is loaded onto network servers. When creating bookmarks and hyperlinks, choose the magnification setting Inherit Zoom so that the destination page displays at the same magnification level that the reviewer is using for the rest of the document.

1.7 Document Information Fields

Document information fields are used to search for individual documents and to identify the document when found. Recommendations for the document information fields are provided below.

- Title: Study title
- Subject: Study type
- Author: Applicant name
- Keywords: Study number, DACO number, animal species

An example of the Document Information field for draft labelling text is provided to the right of this paragraph. Each item of the keyword field should be separated by a comma.



1.8 Open Dialog Box

The open dialog box sets the document view when the file is opened. The initial view of the PDF files should be set as Bookmarks and Page. If there are no bookmarks, set the initial view as Page only. Set the Magnification and PageLayout to default.

1.9 Security

Security settings or password protection for PDF data files should not be enabled. Allow printing, changes to the document, selecting text and graphics, and adding or changing notes and form fields. The PMRA's internal security and archival processes will maintain the integrity of the submitted files.

1.10 Indexing PDF Documents

Full text indexes are used to help find specific documents and/or search for text within documents. When a document or group of documents is indexed, all words and numbers in the file and all information stored in the Document Information fields are stored in special index files that are functionally accessible using the search tools available in Acrobat. Portions of a document that are

presented as an imaged or similar graphic are not indexed. Even if the document only contains images, the text in the Document Information fields of the file will be indexed. These full text indexes should not be confused with a table of contents. Adobe Acrobat Catalog is one example of a tool that can be used to index PDF documents. Indexes should not require extensions or additions to off-the-shelf Acrobat programs. The table of contents file for a section should be associated with the corresponding full text index file. Association means that when the table of contents file is opened, the index file is automatically added to the available index list and is ready to be used.

1.11 Plug-Ins

It is acceptable to use plug-ins to assist in the creation of a Dossier. However, the review of the Dossier by the PMRA should not require the use of any plug-ins, in addition to those provided within the off-the-shelf Acrobat software because the PMRA is not prepared to archive additional plug-in functionality.

2.0 HTML/SGML/XML: Mark-up languages

These formats are under investigation. Further information on these formats can be obtained at

http://www.oasis-open.org/

Annex IV: Desirable alternate data format electronic files and other review aids

Alternate electronic data format files are files provided in addition to those provided for archive of the Dossier. Alternate electronic data format files may contain only the information found in the Dossier, but in a different format. The following text lists some of the alternate electronic data formats which provide PMRA evaluators with additional funtionality.

1.0 Chemical structures

Chemical structures included in the report are preferred in a format which can be opened and edited by ChemWindows. This permits editing of metabolism pathway diagrams to incorporate additional elements, for corrections to be made, and for incorporation of additional annotations/labels. These diagrams are very time consuming to generate de novo.

ChemWindows can import and export several file types. These must have the correct extension to work properly. Placeable Windows Metafile format is not editable and is therefore not acceptable for submission.

Import file type	Export file type
Placeable Windows Metafile (.WMF) ChemIntosh DA (.CW) ChemWindow 1.x/ChemWindowClassic (.CW) ChemConnection (.CW) Standard Chemistry Format (.SCF) MDL MolFile (.MOL) ChemDraw (.CHM)	Placeable Windows Metafile (.WMF) Encapsulated PostScript (.EPS) WordPerfect Graphics File (.WPG) MDL MolFile (.MOL) Standard Chemistry Format (.SCF) ChemDraw (.CHM)

2.0 Spreadsheets

Spreadsheets in versions up to MS Excel 97 and Lotus 97 for IBM PC Windows (not Mac). Calculation formulas should be visible within the spreadsheet. Provision of data in a spreadsheet facilitates re-grouping and/or analysis of data and can significantly reduce evaluation effort. It also permits validation/reproduction of calculations made by the Applicant.

Spreadsheet data is desirable for:

- Complicated data and analysis such as:
  - carcinogenicity tumor incidence tables
  - developmental toxicity effect tables

- Efficacy and Value data
  Frequency and distribution tables, as required under Dir 93-07B and Pro 98-02 Annex VII (table formatting).

Guidance for inclusion of spreadsheet files

- Remove all passwords and locked cells.
- Avoid heavily formatted spreadsheets.
- Include any calculation formulas.
- Fill in all spreadsheet cells to permit sorting without loss of header or title information.
- Name individual worksheets and workbooks to permit rapid access to the data.
  Currently there is no naming convention, but use of a DACO number or a descriptive word or phrase sufficient to identify sheet or workbook contents is sufficient.
- Active DDE or other links between spreadsheet tables or to word processing files is not acceptable at present. Such links may alter data tables when spreadsheets are manipulated by evaluators. Evaluators may not know such changes are occurring.
- Make use of the most recent software version available.
- Avoid converting file formats between software applications (ie between MSExcel and Lotus 123). Conversions will not be absolutely true. This is due to evolving versions/features and conversion utilities which have not captured the latest changes. Lack of fidelity is also due to features unique to any given software package, or to different methods of calculations (Excel and Lotus 123 have a different order of mathematical operation for some operations, potentially altering the outcome of calculations. While Lotus 123 has built a fudge into their conversion utility to account for this, it is unknown if Excel has done the same).

3.0 WordPerfect files

WordPerfect 8.0 is the PMRA's word processing application. Some examples of files which would be of particular benefit to receive as WordPerfect files:

- Tier II Comprehensive Data Summary
- Tier III Comprehensive Data Summary

4.0 Other review aids

New data may not be presented in these alternate format data files. These files may enhance a text description provided in the paper and electronic Dossier.

Videos - Electronic movies should be capable of being displayed on the PMRA minimum standard computer at an acceptable resolution and size, with a

minimum number of hesitations, so that the process or effect being demonstrated is clearly presented.

Photomicrographs - For photographs, the image should be obtained with a resolution of 600 dpi. If black and white photos are submitted, consider 8-bit gray scale images. If colour photos are submitted, consider 24-bit RGB images. A captured image must not be subjected to non-uniform scaling (i.e., sizing). Gels and karyotypes should be scanned directly, rather than from photographs. Scanning should be at 600 dpi and 8-bit grayscale depth.

Annex IV: PMRA informatics environment

LAN Characteristics

The PMRA LAN system operates on Novell 4.11, 10 baseT to individual desktops.

Evaluator Desktop PC's

Minimum configuration: Y2K compliant Pentium, 266 MHz +, 64 Mb RAM, 1 Gb + hard disk, running Windows 95, 17" colour monitors, 24XCD read-only player.

Available software includes:

Word processing:	WordPerfect™ 8
Spread sheets:	Microsoft Excel 97, Lotus 123 97
Browser:	NetScape™ 4.5

Other:
Adobe Acrobat™ 4.0
Adobe Reader™ 4.0
Microsoft Powerpoint™ 97

IT Support

PMRA has a small IT support group, dedicated to LAN and Desktop support. The provision of access by the PMRA to support for electronic Dossiers and its associated software is the responsibility of the Applicant.